Magnetizable Intravascular Stent and Functionalized Magnetic Carriers: A Novel Approach for Noninvasive Yet Targeted Drug Delivery

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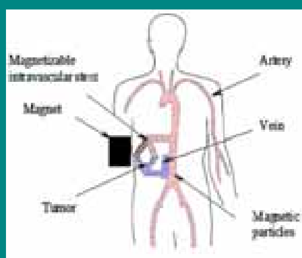
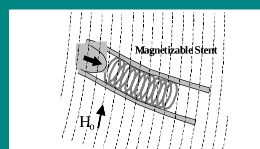
Abstract

A newly devised magnetic drug targeting system (MDTS) based on a hypothetical magnetizable intravascular stent is proposed. A 2-D model is constructed to demonstrate and examine the capture ability of a proposed ferromagnetic intravascular stent. The performance of the magnetizable intravascular stent (MIS) is evaluated in terms of collection efficiency, for which the role of non-stent parameters are evaluated. Parameters include blood velocity (0.02 to 1.2 m s^{-1}); the strength of the applied field (0.05 to 1.0 T); magnetic properties of the magnetic carriers, such as the amount (20 to 80%) and type (iron or magnetite) of ferromagnetic elements in the magnetic carriers and the size of the magnetic carriers (0.5 to 20 mm radius). The results indicate that under most physiological conditions and using current techniques, collection efficiencies as high as 20~50% (sometimes more than 50%) are easily attainable for one cycle. After considering the short circulation period of the circulatory system, relatively high flow rate in large arteries and veins, and the agglomeration of magnetic carriers, the results are remarkable and indicate that a high gradient magnetic separation based MDTS – magnetizable intravascular stent can be an effective tool in collecting magnetic carriers from blood flow in arteries and veins at a target site and offers considerable promise as an effective drug-targeting tool with many potential applications.

Background



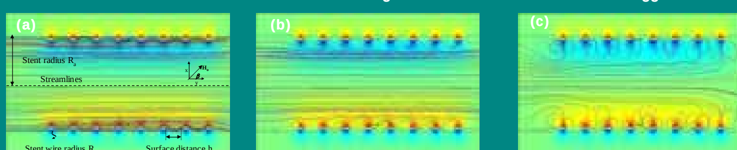


Concept

A magnetizable stent is an array of wires that create high local magnetic field gradients when immersed in a uniform magnetic field; strong forces are generated, causing the magnetic spheres to deflect toward and attach to the magnetized wires.

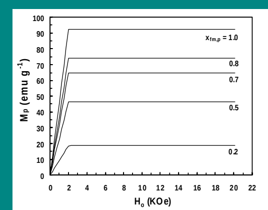
Femlab Results

Blood | 2.0-mm-radius magnetic carriers | 20-mm-radius agglomerates



Results

Magnetization of single (non-porous) magnetic carriers

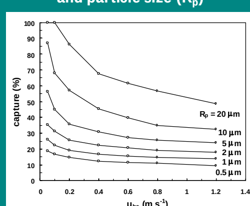


Magnetization ($M_p = w_{fm,p}M_{fm,p}$) of single (non-porous) drug carrier particles as a function of the magnetic field (H_o) and magnetite weight content ($x_{fm,p}$) in cgs units.

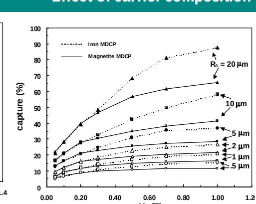
Streamlines of (a) blood, (b) single (non-porous, ε_p = 0.0) drug carrier particles of 2.0 mm radius, and (c) porous (ε_p = 0.4) agglomerates of single drug carrier particles of 20 mm radius through the 8-loop stent and under a field of 1.0 perpendicular to both the plane of the figure and the blood flow. The radius of the stent cross-sectional area (R_a) was 2.5 mm, the velocity of the upstream vessel ($u_{B,0}$) was 0.8 m s^{-1}, the magnetite weight content in single particles ($x_{fm,p}$) was 80%, and the angle of the field (b) was p/2.

Parameter Study

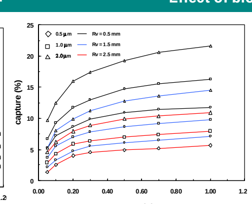
Effect of blood velocity (U_{bo}) and particle size (R_p)

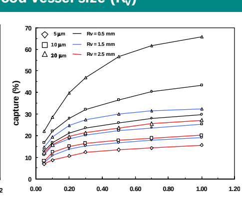


Effect of carrier composition

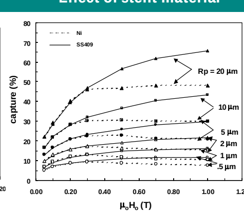


Effect of blood vessel size (R_v)

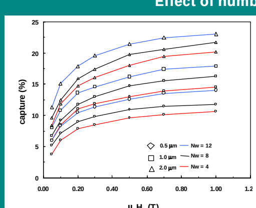


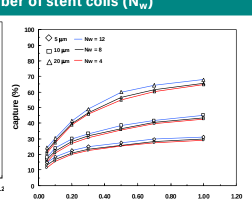


Effect of stent material

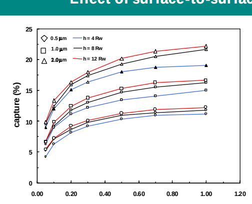


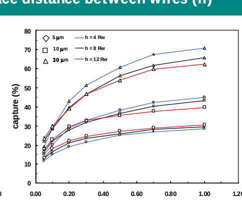
Effect of number of stent coils (N_w)



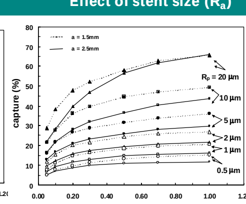


Effect of surface-to-surface distance between wires (h)





Effect of stent size (R_a)



Summary

- Magnetic carriers that are large and/or have high ferromagnetic material content are easily sequestrated by MIS.
- It is recommended to use a MIS that has the same size as the target vessels in order to obtain a better magnetic carrier collection efficiency.
- 400 series stainless steels such as SS409 and SS430 can be good candidate materials for the proposed MIS.
- The number of stent coils number (N_w) is not a significant parameter according to our simulation results.
- The effect of surface-to-surface distance (h) is complicated. A longer stent (larger h with same number of coils) seems to promote the collection of small MDCPs or MDCP clusters; however, for the collection of large magnetic carriers such as 10.0-mm and 20.0-mm magnetic carrier clusters at relative high applied magnetic fields, the shortest stent ($4R_w$) becomes the most efficient.
- Magnetic field direction (β) is not a significant parameter for magnetic carrier collection.
- Larger stent wires are longer-ranged and have a higher magnetic carrier collection efficiency.

Conclusions

- We present a novel drug delivery technology utilizing a magnetizable, intravascular stent useful for **targeted, non-invasive, and long-term drug delivery.**
- After placement of this stent, on-demand systemically injected medicated magnetic particles can be concentrated at the stent site for targeted drug delivery into the surrounding tissue.
- The mathematical modeling of our technology proves the theoretical feasibility of this innovative drug delivery system.

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